

Chapter 1

The Wonderful World of Organic Chemistry

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Organic chemistry is a tyrant you've heard about a lot. You've heard your acquaintances whisper about it in secret. It's mean, they say; it's brutish and impossibly difficult; it's unpleasant to be around (and smells sort of funny). This is the chapter where I introduce you to organic chemistry, and where, I hope, you decide to forget about the negative comments you've heard about the subject.

In this chapter, I show you that the nasty rumors about organic chemistry are (mostly) untrue. I also talk about what organic chemistry is, and why you should spend precious hours of your life studying it. I show you that discovering organic chemistry really is a worthwhile and enjoyable expedition. And the journey is not all uphill, either.

Shaking Hands with Organic Chemistry

Although organic is a very important and valuable subject, and for some it's even a highly enjoyable subject, I realize that organic chemistry is intimidating, especially when you first approach it. Perhaps you've already had what many old-timers refer to simply as The Experience, the one where you picked up the textbook for the first time. This is the time when you heaved the book off the shelf in the bookstore. When you strained your back

trying to hold it aloft. When you felt The Dread creep down your spine as you scanned through the book's seemingly infinite number of pages and feared that, not only would you have to read all of it, but that reading it wouldn't be exactly like breezing through a Hardy Boys adventure or a Nancy Drew mystery.

No doubt, the material appeared strange. Opening to a page halfway through the book you saw bizarre chemical structures littering the page, curved arrows swooshing here and there like flocks of starlings, and data tables bulging with an inordinate number of values — values that you suspect you might be required to memorize. I admit that organic chemistry is a little frightening.

The soap opera of organic molecules

Organic molecules govern our life processes like metabolism, genetic coding, and energy storage. In nature, organic molecules also play out a crazy soap opera, acting as the medium for many twists and turns, deceptions, betrayals, strategic alliances, romances, and even warfare.

Take plants, for example. They seem so defenseless. When a predator comes to lunch on a plant's leaves, the plant can't just pack up its bags and take off. It's stuck where it is, so there's nothing it can do, right? But although plants may seem defenseless, they're not. Many plants produce *antifeedants*, nasty organic compounds that are unpleasant tasting or even toxic to those who would dare eat them. (As a kid, I always *knew* Brussels sprouts contained something like this.) Predators that have feasted on a plant rich in these unpleasant compounds make sure to refrain from eating them in the future.

To produce antifeedants to discourage being eaten is bad enough, but sometimes plants have defenses that seem evil. Certain species of plants, for example, can detect when a caterpillar has decided to munch on its leaves

(by detecting organic molecules present in the caterpillar's spit!). When the plant detects that a caterpillar has decided to make supper on its leaves, the plant emits volatile organic molecules into the air, chemicals designed to attract wasps. When the wasps buzz by to check out what's up, they see the caterpillars eating the plant and killing it. The wasps couldn't care less about the misfortunes of the plant, but the female wasps do need a comfortable spot to hatch their eggs. And what's a snugger nursery than the innards of a fat, juicy caterpillar?

When a wasp spots a caterpillar, it swoops down, makes a crash landing on the caterpillar's back, stings the caterpillar into paralysis, and lays its eggs *inside* of it! When the wasp larvae hatch shortly thereafter, they make the caterpillar their first meal, munching on it contentedly from the inside out. The wasp has now reproduced and has had its little offspring fed, and the plant is rid of its pest — a strange alliance between wasp and plant, all thanks to communication by organic molecules. And that's just one episode in this never-ending soap opera, produced, funded, and sponsored by organic molecules.

I think most students feel this way before they take this class, and probably even your professor did, as did her professor before her. *So you're not alone.* But you can take comfort in knowing that organic chemistry is not as hard as it looks. Those who put in the required amount of work — which, admittedly, is a lot — and don't fall behind, almost always do well. More than almost any other subject, organic chemistry rewards the hard workers (like you), and relentlessly punishes the slothful (the others in your class). I think understanding organic chemistry is not so much hard as it is hard work.



I hope all this talk about how intimidating the course is hasn't put a damper on your enthusiasm, because the subject of organic chemistry really is a doozy. To learn about organic chemistry is to learn about life itself, because living organisms are composed of organic molecules and use organic molecules to function. Swarms of organic molecules are at work in your body — fueling your brain, helping your neurons fire, and getting the muscles in your mouth to clench open and shut — and that's just a small sampling of the organic molecules needed in order for you to complain about your school's chemistry requirements.

Humans, in fact, are composed almost entirely of organic molecules (all the soft parts anyway), from our muscles, hair, and organs, to the fats that cushion our bellies and keep us toasty warm during sweltering summer nights (some people are more richly blessed in this regard than others). Organic molecules can also range in size from the very tiny, like the carbon dioxide you exhale that consists of only three atoms, to the staggeringly large, like DNA, which acts as your molecular instruction manual and is made up of millions of atoms.

What Are Organic Molecules, Exactly?

But what ties all of these molecules together? *What exactly makes a molecule organic?* The answer lies in a single, precious atom: carbon. All organic molecules contain carbon, and to study organic chemistry is to study molecules made of carbon and to see what kinds of reactions they undergo and how they're put together. When these principles are known, that knowledge can be put to good use, to make better drugs, stronger plastics, better materials to make smaller and faster computer chips, better paints, dyes, coatings, explosives, and polymers, and a million other things that help to improve our quality of life.

That said, I should also point out that the field of organic chemistry is essentially an arbitrary one, that the same fundamental laws of chemistry and physics that apply to inorganic molecules apply just as well to organic ones. This connectivity of the branches of chemistry is actually a relatively

new idea, as organic molecules were once falsely thought to have a “vital life force” that other molecules didn’t possess. Despite the destruction of this theory of *vitalism*, chemists still keep the old divisions of chemistry, divisions that define the branches of physical chemistry, inorganic chemistry, and biochemistry. But these barriers are slowly beginning to dissolve, and they’re kept mainly to help students focus on the material taught in a given course.

Given the many elements present in the universe, it is fascinating that living things selected carbon as their building block. So, what makes carbon so special? What makes it better as the foundation for life than any of the other elements? What makes this atom so important that an entire subject focuses around this single atom, while the chemistries of all the other elements are tossed into a big mushy pile known as *inorganic chemistry*? Is carbon really, in fact, all that special compared to the many other elements that could have been selected?

In short, yes. Carbon is very special, and its usefulness lies in its versatility. Carbon has the capability of forming four bonds, so molecules that contain carbon can be of varied and intricate designs. Also, carbon bonds represent the perfect trade-off between stability and reactivity — carbon bonds are neither too strong nor too weak. Instead, they epitomize what chemists refer to affectionately as the *Goldilocks principle* — carbon bonds are neither “too hot” nor “too cold,” but are “just right.” If these bonds were too strong, carbon would be unreactive and useless to organisms; if they were too weak, they would be unstable and would be just as worthless. Instead, carbon bonds straddle the two extremes, being neither too strong nor too weak, making them fit for being the backbone of life.

Also, carbon is one of the very few elements that can form strong bonds to itself, in addition to being able to form bonds to a wide variety of other elements. Carbon bonds can even double back to form rings. Because of this ability to bond with itself and other elements, carbon can form an incredibly vast array of molecules. Millions of organic compounds have already been made and characterized, and undoubtedly many millions more will be discovered (perhaps, dear reader, by you!).

An Organic Chemist by Any Other Name . . .

Just as the field of chemistry can be broken down into different branches, so, too, can the field of organic chemistry be broken down into specialized areas of research. Those who work in these different areas — these specialized “organic chemists” — illustrate the diversity of the field of organic chemistry and its connection to other branches in chemistry, branches like physical chemistry, biochemistry, and inorganic chemistry.

Synthetic organic chemists

Synthetic organic chemists concern themselves with making organic molecules. In particular, synthetic chemists are interested in taking cheap and available starting materials and converting them into valuable products. Some synthetic chemists devote themselves to developing procedures that can be used by others in constructing complex molecules. These chemists want to develop general procedures that are flexible and can be used in synthesizing as many different kinds of molecules as possible. Others devote themselves to developing reactions that make certain kinds of bonds, such as carbon-carbon bonds.

Others use known procedures to tackle multistep syntheses — the making of complex compounds using many individual, known reactions. Performing these multistep syntheses tests the limits of known procedures. These multistep syntheses force innovation and creativity on the part of the chemist, in addition to encouraging endurance and flexibility when a step in the synthesis goes wrong (things inevitably go wrong during the synthesis of complex molecules). Such innovation contributes to the body of knowledge of organic chemistry.

Synthetic organic chemists often flock to the pharmaceutical industry, mapping out efficient reaction pathways to make drugs and optimizing reactions to make complicated organic molecules as cheaply and efficiently as possible for use as pharmaceuticals. (Sometimes improving the yield of the reaction of a big-name drug by a few percentage points can save millions of dollars for a pharmaceutical company each year.) If you take a laboratory course in organic chemistry, you'll be doing a lot of organic synthesis.

Bioorganic chemists

Bioorganic chemists are particularly interested in the enzymes of living organisms. Enzymes are very large organic molecules, and are the worker bees of cells, catalyzing (speeding up) all the reactions in the cell. These enzymes range from the moderately important ones, such as the ones that keep us alive by breaking down food and storing energy, to the really important ones, like the ones in yeasts that are responsible for fermentation, or the breaking down of sugars into alcohol.

These catalysts work with an efficiency and selectivity that synthetic organic chemists can only envy (see the previous section). Bioorganic chemists are particularly interested in looking at these marvels of nature, these enzymes, and determining how they operate. When chemists understand the mechanisms of how these enzymes catalyze particular reactions in the cell, this knowledge can be used to design enzyme *inhibitors*, molecules that block the action of these enzymes.

Such inhibitors make up a great deal of the drugs on the market today. Aspirin, for example, is an inhibitor of the *cyclooxygenase* (COX) enzymes. These COX enzymes are responsible for making the pain transmitters in the body (called the *prostaglandins*). These transmitters are the messengers that tell your brain to feel pain in the thumb that you just smashed with a slip of your hammer. When the aspirin drug inhibits these COX enzymes from operating, the enzymes in your body can no longer make these pain-signaling molecules. In this way, the feeling of pain in the body is reduced. Many other examples of these kinds of inhibitor drugs exist today, and the process of designing these drugs is aided by bioorganic chemists.

Natural products chemists

Natural products chemists isolate compounds from living things. Organic compounds isolated from living organisms are called *natural products*. Throughout history, drugs have come from natural products. In fact, only recently have drugs been made synthetically in the lab. Penicillin, for example, is a natural product produced by a fungus, and this famous drug has saved millions of lives by killing harmful bacteria. The healing properties of herbs and teas and other “witches’ brews” are usually the result of the natural products contained in the plants. Some Native American groups chewed willow bark to relieve pain, as the bark contained the active form of aspirin; other Native American groups engaged in the smoking of peyote, which contains a natural product with hallucinogenic properties. Smokers get a buzz from the natural product in tobacco called nicotine; coffee drinkers get their buzz from the natural product found in coffee beans called caffeine.

Even today, a great many of the drugs found on the shelves of pharmacies are derived from natural products. Once extracted from the living organism, natural products are often tested by chemists for biological activity. For example, a natural product might be tested to see if it can kill bacteria or cancer cells, or if it can act as an anti-inflammatory drug. Often when chemists find a “hit” — a compound that shows useful biological activity — the structures of these natural products are then modified by synthetic organic chemists to try to increase the potency of the compound or to reduce the number of harmful side effects produced by the natural product.

To take another example, after a few decades of use, the natural penicillin isolated from mold ceased to be as effective as an antibiotic, as bacteria developed mechanisms for resistance to this drug, including evolving enzymes that snipped the penicillin molecule into pieces within bacterial cells that rendered the drug ineffective. As a result, synthetic chemists had to synthesize new derivatives of penicillin that still killed bacteria, but bypassed their mechanisms of resistance. Because bacteria eventually

evolve resistance to new molecules, we currently have what amounts to an escalating battle of chemical warfare between humans and bacteria. In this fight, bacteria develop resistance to known drugs and we develop new molecules for the next round of attack. Both synthetic chemists and natural products chemists play a collaborative role in developing more effective antibiotics.

Physical organic chemists

Physical organic chemists are interested in understanding the underlying principles that determine why atoms behave as they do. Physical organic chemists, in particular, study the underlying principles and behaviors of organic molecules. Some physical organic chemists are interested in modeling the behavior of chemical systems and understanding the properties and reactivities of molecules. Others study and predict how fast certain reactions will occur; this specialized area is called *kinetics*. Still others study the energies of molecules, and use equations to predict how much product a reaction will make at equilibrium; this area is called *thermodynamics*. Physical organic chemists are also interested in *spectroscopy* and *photochemistry*, both of which study the interactions of light with molecules. (Photosynthesis by plants is probably the most well-known example of light interacting with molecules in nature.)

Organometallic chemists

Organometallic chemists are interested in molecules that contain both metals and carbon. Such molecules are often used as catalysts for chemical reactions. (Catalysts speed up reactions.) Carbon-carbon bonds are strong compared to carbon-metal bonds, so these carbon-metal bonds are much more easily made and more easily broken than carbon-carbon bonds. As such, they're useful for catalyzing chemical transformations of organic molecules. Many organometallic chemists concern themselves with making and optimizing organometallic catalysts for specific kinds of reactions.

Computational chemists

With the recent advances in the speed of computers, chemists have rushed to use computers to aid their own studies of atoms and molecules. *Computational chemists* model compounds (both inorganic and organic compounds) to predict many different properties of these compounds. For example, computational chemists are often interested in the three-dimensional structure of molecules and in the energies of molecules.

The models generated by computational chemists are getting more and more sophisticated as computers increase in speed and as physical chemists create better models. Many drugs are now modeled on computers by computational chemists; this process is called *in silico* drug design, meaning that the drug is designed in the silicon-based computer. Typically, drugs work by blocking a receptor on an enzyme (see the earlier section on bioorganic chemists). *In silico* drug design focuses on modeling to see which compounds would best fit into the drug's target receptor. This allows for *rational drug design*, or the use of the brain and a molecular model to come up with the structure of a drug instead of simply using the "brute-force methods" that involve testing thousands of randomly selected compounds and looking for biological activity. Computational methods are not sophisticated enough that we can fire all the experimentalists yet (and, perhaps, they may never reach that level of sophistication), but they are useful as a partner to understand, explain, and predict the results from lab experiments.

Materials chemists

Materials chemists are interested in, well, materials. Plastics, polymers, coatings, paints, dyes, explosives — all these are of interest to the materials chemist. Materials chemists often work with both organic and inorganic materials, but many of the compounds of interest to materials chemists are organic. Teflon is an organic polymeric material that keeps things from sticking to surfaces, polyvinyl chloride (PVC) is a polymer used to make pipes, and polyethylene is a plastic found in milk jugs and carpeting.

Materials chemists also design environmentally safe detergents that retain their cleaning power. Organic materials are also required for photolithography to make smaller, faster, and more reliable computer chips. All these applications and millions of others are of interest to the materials chemist.